CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

75-374

CORRESPONDENCE

ALTANA

Altana Inc. 60 Baylis Road, Melville, N.Y. 11747 516-454-7677 Fax: 516-454-6389 BYK GULDEN PHARMA GROUP

Federal Express

October 29, 1998

NEW CORRESP
NC
Noted
gBarnes
11/3/98

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs (HFD-600)
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II, Room 286
7500 Standish Place
Rockville, MD 20855-2773

Re: ANDA 75-374
Diflorasone Diacetate Ointment, 0.05%

Dear Dr. Patel:

Reference is made to your communication of October 9, 1998 in which several deficiencies were noted in our application.

Reference is also made to our October 23, 1998 response. We request that Attachment 1 of our October 23, 1998 response be removed and replaced with the enclosed revised specification. It was noted after the amendment was submitted that the actual specifications for Specific Gravity were somehow omitted from the specification sheet. No other changes have been made to the In Process Specification submitted October 23, 1998.

Thank you for your cooperation in this matter.

If any further information is required, please contact me at 516-454-7677, ext. 2091.

Sincerely,
Altana Inc.

Virginia Carman

Virginia Carman
Associate Director
Regulatory Affairs

OCT 30 1998

VC:pj
Encl.

ALTANA

Altana Inc. 60 Baylis Road, Melville, N.Y. 11747 516-454-7677 Fax: 516-454-6389 BYK GULDEN PHARMA GROUP

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October 23, 1998

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs (HFD-600)
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II, Room 286
7500 Standish Place
Rockville, MD 20855-2773

Re: ANDA 75-374 **MAJOR AMENDMENT**
Diflorasone Diacetate Ointment USP, 0.05%

Dear Dr. Patel:

Reference is made to our original Abbreviated New Drug Application submitted May 1, 1998 pursuant to Section 505(j) of the FDC Act.

Reference is also made to the Agency's letter of October 9, 1998 in which several deficiencies were noted in our application.

We wish to respond to the Agency's concerns as follows:

A. Deficiencies

Comment

1. Based on your data, please revise your in-process and finished product acceptance limits for degradation products.

Response

We have tightened our in process and finished product acceptance limits for degradation products. Revised in process specifications may be found in Attachment 1. Revised finished product specifications may be located in Attachment 2.

Comment

2. Please tighten the viscosity acceptance limits for release of the finished drug product and stability.

Response

Tightened viscosity limits have been set for the finished product release testing and stability studies. As noted in our response to Comment 1, revised finished product specifications are located in Attachment 2. Revised stability specifications are located in Attachment 3.

Comment

3. Based on your stability data, please revise the acceptance limits for the degradation products. You have reported no degradation in all of your stability data.

Response

The specifications were revised as requested. Although no degradation products were evident during the stability studies, the specifications for the drug substance raw material allow some impurities to be present. Since these impurities may be present in future lots, the specifications for the ointment were tightened with this in mind and provide for but a small amount of degradation beyond the levels which may be present initially in the drug substance. The revised stability specifications can be found in Attachment 3 (Response to Comment 2).

Comment

4. Please revise your in-process controls to include test, procedure and acceptance limits for blend uniformity analysis of the drug product.

Response

In process specifications have been revised to include acceptance limits for blend uniformity analysis of the product. These revised specifications can be found in Attachment 1 (Response to Comment 1).

Comment

5. Please explain the specifications for the homogeneity test.

Response

The specifications for homogeneity require that the individual assay values from the beginning, middle and end of the a tube be within , of the mean of the assay values for the beginning, middle and end of the tube.

Comment

6. Please revise your specifications for glyceryl monosterate to include test, procedure and acceptance limits for organic volatile impurities.

Response

Revised specifications for glyceryl monostearate may be found in Attachment 4. Revised analytical procedures for glyceryl monostearate, non NF are included in Attachment 5.

Comment

7. Please explain the reason for not using the grade of glyceryl monostearate.

Response

Please see the report found in Attachment 6 which explains the rationale for using non NF material as well as differences in several grades of glyceryl monostearate tested.

Comment

8.

Response

Again, there are many grades of glyceryl monostearate available. The glyceryl monostearate was chosen because as noted previously, it gave the See Attachment 6.

Comment

9. Please explain why you need a in your stability specifications. Your data does not support such a limit. Why do you expect a

Response

During extended storage at elevated temperature while undergoing accelerated stability studies, small amounts of the liquefied ointment may be lost from the tube crimp. The specifications have been tightened from to reflect the small losses. See revised stability specifications found in Attachment 3.

Comment

10. Please provide all available room temperature stability data since trends were apparent in the provided data.

Response

Attachment 7 contains 18 month room temperature stability data.

In addition to the responses to the noted deficiencies, we also acknowledge:

1.) The firms referenced in our application should be in compliance with CGMP's at the time of approval; and

2.) Our bio study is under review and further comments may result.

Labeling Deficiencies:

Comment

1. Container (15 g, 30 g, 60 g)
Satisfactory in draft.

Response

Attachment 8 contains final printed container labeling.

Comment

2. Container (15 g, 30 g, 60 g)
Satisfactory in draft.

Response

Attachment 9 contains final printed carton labeling.

Comment

Insert

3. A. Description

Revise the third paragraph to read – Each gram of diflorasone diacetate ointment, for topical administration, contains....

B. Precautions

i. Information for patients

Revise the first bullet to read – This medication.....

ii. Pregnancy

Revise to delete the ultimate sentence, "Drugs of this class...."

C. Dosage and Administration

Revise the first sentence of the first paragraph to read – Diflorasone diacetate ointment should....

D. How Supplied

Revise to include – "Keep tightly closed."

Response

Attachment 10 contains final printed insert labeling.

As further requested, side-by-side comparison of the proposed final printed labeling and our originally submitted labeling may be found as follows:

Attachment 11 – Container labeling
Attachment 12 – Carton labeling
Attachment 13 – Insert labeling

We do acknowledge that the Agency reserves the right to request additional changes in our labels and/or labeling based upon changes in the innovator labeling, or further review of the application prior to approval.

We trust that with this additional information the Agency will deem our application approvable.

If there are any additional questions, please contact me at 516-454-7677, ext. 2091.

Sincerely,
Altana Inc.

Virginia Carman

Virginia Carman
Associate Director
Regulatory Affairs

VC:pj
Encl.

ALTANA

Altana Inc. 60 Baylis Road, Melville, N.Y. 11747 516-454-7677 Fax: 516-454-6389 BYK GULDEN PHARMA GROUP

May 15, 1998

Ms. Denise Huie
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855

VIA TELEFAX (301) 594-1174
AND FEDERAL EXPRESS

Diflorasone Diacetate Ointment USP, 0.05%
ANDA 75-374
Facsimile Amendment

Dear Ms. Huie:

Reference is made to the abbreviated new drug application for Diflorasone Diacetate Ointment USP, 0.05%, ANDA 75-374 submitted on May 1, 1998 pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act.

Altana Inc. is submitting this Amendment in response to the FDA telephone request on May 14, 1998. The information is presented in **comment**/response format.

Reconciliation for the Executed Batch Record: How much bulk product was manufactured and how was it distributed between the 15, 30 and 60 gram tubes?

The reconciliation for the Diflorasone Diacetate Ointment USP, 0.05% exhibit batch Lot #9368 can be found on page 1745 of the original ANDA submission. For ease of review a copy of this page and a summary of the reconciliation have been included in this amendment.

If you require any additional information please contact me at (516) 454-7677 extension 2092.

Sincerely,

Altana Inc.

Cynthia I. Renger
Associate Director, Regulatory Affairs

CIR/ab

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